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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,036	07/30/2001	Kiran Madura	266/165	1466
34055	7590	11/26/2004	EXAMINER	
PERKINS COIE LLP POST OFFICE BOX 1208 SEATTLE, WA 98111-1208			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/918,036

Applicant(s)

MADURA, KIRAN

Examiner

Malgorzata A. Walicka

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,7 and 9-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6,7 and 9-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1652

Reply under 37 CFR 1.111 filed September 9, 2004 is acknowledged. Amendments to the claims and specification have been entered. Claims 1-5 and 13-18 have been cancelled as drawn to the non-elected invention. Claims 6, 9, 10 and 12 have been amended and claim 8 has been canceled in this Reply.

Detailed Action

1. Objections

The objection to the specification for lack of the cross-reference to the previous application and patent is withdrawn, because the specification has been corrected.

Claim 6 in its preamble recites "a cell". Claim 10 recites the term "target cell". It is understood that the use of DNA of claim 6 is in the method of claim 10, both claims, therefore should recite the same term "cell".

2. Rejections

2.1. 35 USC, section 112, second paragraph

Rejection withdrawal

Rejection of the base claim 10 and dependent claims for being unclear in reciting "the half-life of said fusion gene" is moot because the recitation has been cancelled from the claim.

Rejection of claim 10 for use of the relative terms "short", "rapidly" and "longer", which render the claim indefinite is withdrawn, because the claim has been amended.

Art Unit: 1652

New rejection

Claim 6, 7 and 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rejected because neither the claims nor the specification define the term "proliferative potential". For examination purposes it is assumed that a cell has a proliferative potential when it initiates an exponentially growing culture.

2.2. 35 USC, section 112, first paragraph**2.2.1. Lack of written description**Rejection withdrawal

Rejection of claims 10-12 for lack of description of assessing the half-life of any fusion protein in a malignant cell is withdrawn, because the base claim 10 has been amended.

Rejections maintained or caused by amendment

Claim 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the claims are directed to a large genus of methods using a large genus of DNA molecules encoding fusion proteins comprising any ubiquitin like domain and any reporter protein. The structure of the DNA molecules encoding fusion proteins used in the method is not sufficiently described. Provision of nucleic acid molecules that encode Ubl of SEQ ID NO: 2-11 is not sufficient for identifying all the species of the claimed DNA molecules

Art Unit: 1652

encoding fusion proteins comprising any ubiquitin like domain. Given the lack of identifying structural characteristics of the genus of Ubl domain component of the DNA molecules to be used in the method, Applicants have failed to sufficiently describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention when the application was filed.

Claim 6, 7 and 9-12 are rejected for lack of sufficient description of assessing the proliferative potential of a cell. Applicants disclose, for example in Figure 6A, 7A and 9B, that Rad23¹⁻³⁶⁹, Rad23-HA and Ubl^{R23}-lacZ are not detected within 0-30 min. after labeling. These data are not sufficient to be a base for any routine determination as necessary in a claimed method. The kinetics of degradation of the fusion protein containing Ubl domain and a reporter protein seems to depend on cell used and details of measurements, as well as on the fusion protein itself. All of the elements are not sufficiently disclosed. Actually, some of Applicants and other's data indicate that degradation is the same in both exponential and stationary-phases of growth (page 32 line 26 of the specification); see also the data for the cells temporarily arrested in their growth, page 33, line 34 of the specification. In addition, as taught by the specification, some exponentially growing cells do not degrade fusion proteins comprising Ubl and a reporter gene; see results for ufd5Δ mutant (Fig. 10E), page 36, line 13, cim5-1 cells (Fig. 11B) page 37, line 6 and pre1-1 pre2-2 cells (Fig. 11A), page 37, line 13. Thus,

Art Unit: 1652

the one skilled in the art is not convinced that Applicants were in possession of the claimed invention at the time the application was filed.

In Remarks, on page 11, second paragraph, Applicants argue, "MPEP 2163.02 indicates that 'objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.' In re Gosteli, 872 F. 2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)." This argument has been fully considered but is not persuasive. In the light of the facts taught in the specification as presented above, one of ordinary skills in the art cannot recognize that the inventors invented what is claimed.

2.2.2. Scope of enablement

Claim 6-7 and 9-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for degradation of Rad23¹⁻³⁶⁹, Rad23-HA and Ubl^{R23}-lacZ within 0-30 min. after labeling when the labeling is performed in some exponentially growing yeast transformants (Fig. 7 and 9), does not reasonably provide enablement for assessment of a proliferative potential of any cell using any fused DNA encoding a protein consisting of any Ubl domain and a reporter protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Art Unit: 1652

The claims are directed to a method for assessing the proliferative potential of cells by using DNA constructs encoding fusion proteins whose function is to be used in said method. The specification, however, is not enabling for use of any DNA encoding for the fusion protein when said fusion protein consists of any Ubl domain or Ubl domain of sequences listed in claim 6 and 11 and for any cell for which the measurement is to be performed.

Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any DNA construct encoding for Ubl-reporter, wherein Ubl is any one of SEQ ID NO: 2-11 operably linked to any reporter, or any Ubl operably linked to reporter that is identified by claims 9 and 12 wherein said proteins are used in a method of assessing the proliferative potential of any cells.

The art of construction of DNA molecules encoding for fusion proteins is highly developed and skills of artisan high, however, because the structure of the claimed fusion polypeptide to be used, and the method of use itself, are lacking enabling

Art Unit: 1652

description (see the above rejection for lack of written description), one skilled in the art is forced to perform undue experimentation with low probability of success.

Since the degradation of any fusion protein in any multiplying cell, is not disclosed, one skilled in the art would not know which fusion protein, i.e. its encoding DNA, and which cell type to select for the method. As exemplified in the specification for yeast cells (*Sacharomyces cerevisiae*) the mechanism of degradation of fusion proteins is complex and involves so called N-end rule pathway and UFD pathway (Ub fusion degradation). Degradation of a particular Ubl-reporter depends on these two pathways and is affected by mutations in any of the genes in the pathways. The degradation also depends on primary and mutated structure of a Ubl used for fusion. In addition, the degradation depends on the link between the Ubl and the reporter. US patent 5,132,213 (quoted by examiner in the last Office action) discloses in Table 2, column 18 that the construct Ubl-Lys- β gal has in *S. cerevisiae* the half-life of 3 min, but Ubl-Met-Lys- β gal more than 20 h; see Fig. 6 of the Patent. Thus, the half-life of any particular construct depends on its structure. In addition, Applicants themselves teach that whereas some yeast cells in logarithmic phase degrade the fusion proteins, other yeast cells do not degrade said fusion protein when they are in the exponential phase of culture; see the above rejection for lack of written description. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the fusion proteins had the function to be used in the method for assessing the proliferative potential of

Art Unit: 1652

particular cells. The disclosure fails to provide such guidance of the structure of DNA encoding fusion proteins and the guidance as to the type of cells for which the use of said DNA is applicable; in result, experimentation left to those in the art is improperly extensive and undue.

2.3. 35 USC section 102

Rejection of claim 6, 7 and 9 under 35 U.S.C. 102(b) as being anticipated by the US Patent 5,132,213 is withdrawn, because the claims have been amended.

3. Conclusion


All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (571) 272-0944 and the right fax number is (571) 273-0944. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m. EST.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.
Art Unit 1652
Patent Examiner


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